REMARKS

Claims 83-130 are presently pending. Claims 38-76, 78-82 were previously cancelled, and claims 1-37, 77 were previously withdrawn. Claims 127-130 are presently withdrawn. Minor amendments have been made to the specification and claims to simply overcome the objections to the specification and rejections of the claims under 35 U.S.C. § 112. Amendments have been made to claims 83, 91, 96, 100, 110, 113, 114, 121, 124, and 126. The Examiner is respectfully requested to reconsider and withdraw the rejection(s) in view of the amendments and remarks contained herein.

SEQUENCE LISTING

Item 7. A Sequence Listing, a computer readable form of the Sequence Listing and a Statement under 37 CFR 1.821-1.825 is provided with this amendment. Attached also, the Examiner shall find the Notice to Comply Form along with the Applicants' Notice to Comply response.

SPECIFICATION

Item 8. The specification is objected to because it does not provide sequence identifiers for the following primer sequences and linker sequence pursuant to 37 CFR 1.821(c) and/or (d): Primer- p. 20, [0049]; p. 21, [0050-0051]; p. 22 [0054]; p. 24, [0056] and p. 39, [00105]; and Linker- [0029] and figures 8-11.

Applicants have amended the specification herein to provide sequence identifiers for the following primer sequences: Primer- p. 20, [0049]; p. 21, [0050-0051]; p. 22 [0054];

p. 24, [0056] and p. 39, [00105]; and Linker- [0029] and figures 8-11 pursuant to 37 CFR 1.821 (c)and/or (d). Applicants respectfully request withdrawal of the present objection.

Item 9. The specification is objected to because there appears to be an obvious typographical error:"C□3". Applicants have amended paragraph [0038] to correctly state "Cγ3". Applicants respectfully request withdrawal of the present objection.

Item 10. The specification is objected to because the use of trademarks in paragraph [00105] appear inadvertently misquoted. Applicants have amended paragraph [00105] to capitalize the trademark, followed by citation in parenthesis of the generic version as recommended by the Examiner. Applicants respectfully request withdrawal of the present objection.

CLAIM OBJECTIONS

Item 11. Claims 96, 97, and 124-126 are objected to as being drawn to non-elected subject matter for the species HLA, CD14, and a toll-like receptor (claim 96), a subspecies HLA-DP (claim 97) and an infectious disease (claims 124-126).

Claim 96 has been amended to delete the non-elected subject matter for the species HLA, CD14, and a toll-like receptor, and CD40 and have kept the elected subspecies chemokine receptor.

Claim 97 has been withdrawn and amended to recite the targeting units of claim 83 having the ability to target the non-elected subspecies HLA or HLA-DP, CD14, a toll-like receptor, and CD40. Support for this amendment can be found in the specification, for example, on pages 14, 24, and original claims 4-8.

Claim 124 has been amended to recite a vaccine composition comprising a nucleic acid according to the claim 83 further defining the immunologically effective aspect of the vaccine. Support for this amendment can be found on page 56.

REJECTION UNDER 35 U.S.C. § 112

Item 12. Claims 91, 100, 110, 113, 114, 121 and 124-126 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point and distinctly claim the subject matter which Applicants regard as the invention.

Claim 91 is allegedly found indefinite for the recitation of "MIP-1α". Applicants have amended the term as recommended by the Examiner to "Macrophage Inflammatory Protein 1 alpha" Applicants respectfully request withdrawal of the present rejection.

Claims 100, 110, and 114 have been allegedly found as indefinite for recitation of the term "derived". Applicants have deleted the term "derived" from claims 100, 110 and 114. Applicants have replaced "derived from" to more clearly state: "identical to" with reference to the antigenic scFv sequence obtained from myeloma or lymphoma monoclonal Ig molecules. Support for this amendment can be found on page 15. Applicants respectfully request withdrawal of the present rejection.

Claim 113 has been found to be allegedly indefinite by the recitation of the term "substantially". Applicants have amended claim 113 to delete this term to render this rejection moot.

Claims 121 and 124-126 have been found to be allegedly indefinite by the phrase "degenerate variant thereof". Applicants have amended claims 121, and 124-126 by

deleting the term "degenerate" and/or "variant" to more clearly define the subject matter of the claims. Applicants by deleting these terms, have rendered the present rejection moot.

Item 13. Claims 118, 121, 122 and 124-126 are rejected under 35 U.S.C. § 112 allegedly because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. This rejection is respectfully traversed.

Claims 118, 121, 122 and 124-126 relate to nucleic acids and vectors that are formulated for immunization rather than by delivery via a gene therapy route. As stated in the specification at paragraph [0040] on page 16:"Immunization by means of Vaccibody protein, Vaccibody DNA, or Vaccibody RNA, the latter two executed e.g. by intramuscular injection followed by electroporation (See Examples), are all feasible methods." With respect to Claims 118, 121, 122 and 124-126, the Applicant points to the distinguishable method of genetic immunization rather than by gene therapy. The Action alleges that the specification is not enabling. In support of the Examiner's allegation, the action alleges that the specification does not teach methods of treating or preventing a cancer or induce a protective T- or B-cell immune response in a patient with the nucleic acid, the vector comprising the nucleic acid or a vector transformed cell or cell line.

The specification is replete with examples teaching one of ordinary skill in the art how to prepare the nucleic acids, the vectors comprising the nucleic acids and the vectors and cell lines containing the nucleic acids for administration into patients,

including rodents and humans. See Materials and Methods, pages 20-25. In vivo experiments using mice to determine the Vaccibody response to specific myeloma monoclonal Ab antigenic V region genes MOPC315.4 were shown in the Methods and Materials section pages 20 to 30. Tumor reduction was also shown in mice by challenging the mice using MPRC315.4 cells after DNA Vaccibody administration as shown on pages 28-30. Furthermore, Applicants have clearly demonstrated how to make and use the invention in the exemplified methods provided in Examples 1-13 to demonstrate that the Vaccibodies encoded by the nucleic acids and contained in the compositions of the present invention were capable of inducing an immune response against multiple myeloma and the feasibility of treating mammals including humans by immunization by means of Vaccibody DNA or Vacccibody protein immunization. See pages 30-38.

Genetic immunization with recombinant nucleic acids was an established technique and practiced before the priority date of the present application. It was well known in the art how to administer and test for the presence of anti-Id antibodies specifically produced by intramuscular injection or electroporation of nucleic acids to induce humeral and cellular immune responses in mammals, including humans. See as an example, U.S. Patent No. 5,580,859 (Felgner et al.).

Moreover, the Examiner's arguments based on the article authored by Vile *et al.* is not directly on point to the present technology of this application. However, it is important to note that the Vile et al. reference deals with gene therapy, and not with genetic immunization. Genetic immunization (also known as gene immunization, genetic vaccination, DNA vaccination etc) is a technology which only superficially

resembles gene therapy. Where gene therapy relies on introduction into a cell of genetic material which must be expressed so as to be biologically active in said cell, genetic immunization merely requires the introduction of genetic material in a cell which then has to be expressed in the cell. The gene product can be a secreted or transmembrane expression product. The remaining effector mechanisms rely on the human immune system, because the expression product simply has to be able to induce an adaptive immune response. So, in contrast to gene therapy, genetic vaccination does not require that tumour cells take up a genetic construct; for example, an adenoviral vector: instead it is typical to use skeletal muscle cells as the *in vivo* expression system and it is simpler to ensure that muscle cells are targeted to take up the genetic construct (e.g. via injecting the expression plasmids directly into muscle tissue) than it is to ensure that a tumour cell (which can have an unknown anatomic location) internalizes the genetic material and expresses the same type of construct. In brief, genetic immunization substitutes the traditional administration of immunogenic proteins, peptides, or other antigens such as viral or bacteria or components thereof with administration of genetic material encoding immunogenic proteins. The genetic material described herein can be typically introduced via transient transfection into non-dividing cells (typically skeletal muscle cells), which then express the genetic material. Subsequently, the expression products are recognized by the immune system which then mounts a traditional immune response against the expression product.

Further, a significant number of scientific papers have discussed the genetic immunization, for example, Stevenson *et al.* 2004 (from PNAS, attached as a courtesy copy herewith) which describes more recent experiments with DNA vaccination.

The Examiner's assertion that targeted delivery of vectors by gene therapy; for example, intravenous delivery of viral vector can be problematic in certain circumstances is well taken. However, the present disclosure relates to genetic administration via immunization methods that allow transient transfection of the nucleic acids at the site of injection, typically in non-dividing cells (muscle cells). Furthermore, several scientific papers and patents relating to DNA vaccination prior to the earliest priority date of the present application describe how to utilize the genetic immunogens and their administration routes. Intramuscular immunization of genetic material and coding antigens of interest has been used for more than 15 years, a fact which is also reflected in the scientific documents cited on pages 15 and 16 in the present specification.

REJECTION UNDER 35 U.S.C. § 102

Item 14. Claims 83, 88-92, 96, 98, 109-117, 119, 120 and 123 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Herman (U.S. Publication No. 20050069549; published March 31. 2005; filed January 14, 2003). This rejection is respectfully traversed.

Herman generally relates to multispecific ligands having at least a first ligand binding moiety and a second binding moiety. For example par. [0107] recombinant scFvs including dimmers, trivalent or other multivalent antibody formats, or any truncated form of ligand binding entity. Such antibody can comprise at least a VH or VL portion or both or a functional portion of same.

Herman fails to recite "a monomer unit of a recombinant antibody-based dimeric molecule, wherein said antibody-based dimeric molecule comprises two of said monomer units connected through a dimerization motif, said dimerization motif comprising a hinge region and a Cγ3 domain of each monomer unit, wherein each hinge region contributes to dimerization via disulfide bridging to the other hinge region and each Cγ3 domain contributes to dimerization via hydrophobic interactions to the other Cγ3 domain, and wherein said monomer units each comprises an antigenic unit and a targeting unit for an antigen presenting cell, and wherein said monomer units each lack a CH2 domain". Such constructs are not taught in Herman, and hence the presently claimed subject matter is distinguished over Herman. Applicants have amended claim 83 to a monomer structure having two monomer units, each unit connected through a dimerization motif comprising a hinge region and a Cy3 domain of each unit and each monomer unit lacking a CH2 domain.

Applicant asserts that Herman does not disclose all of the recited features of the presently amended claim 83. For the reasons stated above, dependent claims 88-92, 96, 98, 109-117, 119, 120 and 123, are also not anticipated by Herman.

OTHER REMARKS

Applicants' representative amends the specification to include the sequence listing provided herewith. Please enter the enclosed sequence listing into the application following page 44. No new subject matter has been added.

In addition, submitted herein is a CD containing computer readable form of the sequence listing for the above-referenced patent application in compliance with the

requirements of 37 CFR 1.821, 1.822 and 1.823.

I hereby state that the sequence listing information recorded in computer readable form is identical to the written (paper version) sequence listing being submitted herein in accordance with 37 C.F.R. 1.821(f).

CONCLUSION

It is believed that a full and complete response has been made to all of the issues raised in the outstanding Office Action. Thus, prompt and favorable consideration of this amendment is respectfully requested. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (248) 641-1600.

Respectfully submitted,

Dated: May 7, 2007

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